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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,048	05/01/2001	YongQi Mu	P-091-R	5200

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,048	MU, YONGQI	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,16,17 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16,17 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/8/02*. ; 3/26/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 13, 14, 16, 17 and 20-23 are pending.

Applicants' amendment filed February 6, 2004 is acknowledged, and applicants' response has been fully considered. Claims 20 and 21 have been amended, thus, claims 13, 14, 16, 17 and 20-23 are examined.

Supplemental Information Disclosure Statement

2. All the references listed in the IDS filed January 8 and February 26, 2002 have been considered and initialed, see attached copies.

Objection Withdrawn

3. The previous objection to the disclosure is withdrawn in view of applicants' response at pages 5-6 in the amendment filed February 6, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13, 14, 16, 17 and 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a glycopeptide of formula (II), wherein R^{20} is R^a-W-R^h, W is -S-C(=O)-, R^a and R^h each has a defined structure (see pages 17- 22 of the specification); a pharmaceutical composition comprising the glycopeptide; and a method of treating a mammal having a bacterial disease by administering the glycopeptide or the pharmaceutical composition comprising the glycopeptide, does not reasonably provide

enablement for a glycopeptide of formula (II), wherein R^{20} is R^a-W-R^h, W is -S-C(=O)-, and R^a and R^h each is a substituted group and the structure of the substituent is not defined; a pharmaceutical composition comprising the glycopeptide; and a method of treating a mammal having a bacterial disease by administering the glycopeptide or the pharmaceutical composition comprising the glycopeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 13, 14, 16, 17 and 20-23 are directed to a glycopeptide of formula (II), wherein R^{20} is R^a-W-R^h, W is -S-C(=O)-, and R^a or R^h is a cited group either substituted or not substituted; a pharmaceutical composition comprising the glycopeptide; and a method of treating a mammal having a bacterial disease by administering the glycopeptide or the pharmaceutical composition comprising the glycopeptide. The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides novel disulfide or thioester glycopeptide derivatives, e.g., glycopeptides of formula (II), where R^{20} is R^a-W-R^h and W is -S-S- or -S-C(=O)-, having highly effective antibacterial activity and an improved mammalian safety profile, more specifically, the disulfide or thioester glycopeptide derivatives exhibit reduced tissue accumulation and nephrotoxicity when administered to a mammal, (page 2, line 24-page 3, line 2; pages 13-15). There are no indicia that the present application enables the full scope of claims in view of the thioester glycopeptide compounds and the method of treating a mammal having a bacterial disease by administering the thioester glycopeptide compounds as discussed in the stated rejection. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858

F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding R^a and R^h having various substituted groups in glycopeptide compounds and the effects of the glycopeptides in the treatment of various bacterial diseases, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed variants and the methods in association with the variants, the specification has not demonstrated a thioester glycopeptide compound being isolated and used for treating various bacterial diseases. The specification only indicates the mass spectrum data of four disulfide glycopeptide compounds (Table 1 and Example 1).

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., references at page 2 of the specification) indicates a number of vancomycin or other glycopeptides have been made and used as antibiotics. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on the identities of thioester glycopeptide compounds with various substituted R^a and R^h, and the effects of the compounds in the treatment of various bacterial diseases to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass various thioester glycopeptide compounds and a method of treating a mammal having a bacterial disease by administering the glycopeptide compound, however, the identities of thioester glycopeptide compounds with various substituted R^a and R^h, and the effects of compounds in the treatment of bacterial diseases are not adequately described in the specification, the invention is highly unpredictable regarding the effects of various thioester glycopeptide compounds.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a glycopeptide of formula (II), where R^{20} is R^a-W-R^h and W is -S-C(=O)-, a pharmaceutical composition comprising the glycopeptide, and a method of treating a mammal having a bacterial disease by administering the glycopeptide or the pharmaceutical composition comprising the glycopeptide. The specification indicates a glycopeptide such as vancomycin can be reductive alkylated using an aldehyde to give a glycopeptide that is alkylated at the saccharide-amine (pages 37-38), and aldehydes comprising a thioester group are either commercially available or can be prepared according to Scheme 2 (pages 42-43). The specification further disclose various pharmaceutical formulations comprising the glycopeptides (pages 44-54), preparation of disulfide glycopeptide compounds (Example 1), in vitro and in vivo determination of antibacterial activity of the test compound (Example 2); and determination of tissue accumulation of the test compound (Example 3). However, the specification has not identified a thioester glycopeptide compound having various substituted R^a and R^h, nor has demonstrated the effect of the compound in the treatment of various bacterial diseases.

Moreover, there are no working examples indicating the effects of thioester glycopeptide compounds containing R^a and R^h with various substituents. Since the specification fails to provide sufficient teachings on the identities of thioester glycopeptide compound with R^a and R^h having various substituted groups, and the effect of the compound in treating bacterial diseases, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various thioester glycopeptide compounds in the claimed method.

(6). Nature of the Invention

The scope of the claims encompasses thioester glycopeptides with various R^a and R^h and a method of treating a mammal having a bacterial disease by administering the glycopeptide, but the specification does not demonstrate the effect of the thioester glycopeptide in the treatment. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, there are no working examples demonstrating the claimed variants and methods, the teaching in the specification is limited, and the effect of compound is not indicated, and therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various thioester glycopeptide compounds in the treatment of bacterial diseases.

In response, applicants indicate R^{20} is not exceptionally broad since R^{20} only recites one possibility, R^a-W-R^h, where W is -S-C(=O)-, and R^a and R^h are clearly defined in the specification; there is no requirement for working examples to fulfill the requirements of 35 U.S.C. 112, first paragraph, if the invention is disclosed so that one of ordinary skill in the art can practice the invention without undue experimentation; the scope of the enablement provided by applicant needs only bear a 'reasonable correlation" to the scope of the claims, e.g., the

specification provides general schemes for the preparation of the claimed glycopeptide compounds, and discloses the claimed glycopeptides are highly effective antibacterial agents; and different glycopeptides of formula II would have to be prepared and screened to identify those have anti-bacterial effect does not constitute "undue experimentation" particularly in an art where the level of skill is high, thus given applicants' disclosure and the skill of the art worker in the relevant art area, the preparation and screening of glycopeptides of formula (II), where R^{20} is R^a-W-R^h, and W is -S-C(=O)-, is well within the skill of the art and would not require undue experimentation (pages 6-9 of the response). The response has been considered, however, the argument is not fully persuasive because the specification has only described certain substituents in R^a and R^h of glycopeptides, while the claims encompass numerous undefined variants for glycopeptides of formula II, thus the full scope of the claim is not enabled as indicated in the section above. Furthermore, the claims encompass substituted group in R^a and R^h of glycopeptides without structural definition of substituents, one skilled in the art would not know how to identify an active glycopeptide of formula II without additional guidance on the structures of R^a and R^h of glycopeptides, and without carrying out further experimentation for in vivo treatment. The undue experimentation is necessary since there is no working example and sufficient teachings on the identities of glycopeptides of formula II with R^{20} being R^a-W-R^h, and W being -S-C(=O)- and on the in vivo effects of these glycopeptides for treating various bacterial diseases as indicated in the section above.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13, 14, 16, 17 and 20-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 13, 14, 16, 17 and 20-23 are indefinite because of the use of the term "substituted alkylene", or other cited substituted group. The term "substituted alkylene", or other cited substituted group renders the claim indefinite, it is unclear what substituent is used, where is the substituent located in the group, and what structure the substituted group has, although the specification indicates certain groups can be used as the substituent (page 18, lines 19-page 19, line 9). Claims 14, 16, 17 and 20-23 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

7. Claims 20 and 21 are indefinite because the claim lacks an essential step in the method of treating a mammal having a bacterial disease. The omitted step is outcome of the treatment.

In response, applicants indicate the claim has been amended to cite the term "thereby treating the disease" (page 6 of the response). The response has been fully considered, however, the argument is not found persuasive because the recited term does not show the outcome of the treatment, it is not clear whether the treatment is effective.

Conclusions

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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April 8, 2004

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